SENTARA HEALTH PLANS, INC.
CLINICAL CARE SERVICES

Medical Policy:	**Medical 34 C**	
Subject:	**Genetic Testing 34 C**	**Cardioneurovascular and Developmental Diagnosis**
	See Genetic Testing 34 A	Cancer Prevention, Diagnosis and Treatment
	See Genetic Testing 34 B	Pre-Treatment or Post Intervention
	See Genetic Testing 34 D	Preconceptional /Prenatal /Preimplantation Genetic Testing for Preconceptional /Prenatal /Preimplantation
	See Genetic Testing 34 E	Pharmacogenetic Testing
	See Genetic Testing 34 F	Medicare Coverage
Effective Date:	February 2009	
Review Date:	02/10; 11/15; 5/17, 10/19	
Revised Date:	November 2009; 4/10; 11/10; 01/11; 02/11; 03/11; 4/11; 5/11; 6/11; 7/11; 8/11; 9/11; 10/11; 11/11; 12/11; 01/12; 2/12; 3/12; 4/12; 5/12; 6/12; 7/12; 8/12; 9/12; 10/12; 11/12; 12/12; 1/13; 2/13; 3/13; 4/13; 5/13; 6/13; 7/13; 8/13; 10/13; 11/13; 12/13; 1/14; 2/14; 3/14; 4/14; 5/14; 6/14; 7/14; 8/14; 9/14; 10/14; 11/14; 12/14; 1/15; 2/15; 3/15; 4/15; 5/15; 6/15; 7/15; 8/15; 9/15; 10/15; 11/15; 12/15, 1/16, 2/16; 4/16; 5/16; 6/16, 8/16, 9/17, 3/18, 10/19, 12/19, 1/20, 3/20, 5/20, 6/20, 9/20, 10/20, 12/20, 5/21, 9/21, 2/22, 3/22, 5/22, 8/22, 11/22	

Covered: **See appropriate benefit document for specific coverage determination**

Exceptions: **Based on current scientific evidence, the requested test is considered not medically necessary because the results of genetic testing have not been scientifically shown to improve clinical outcomes:**

- ACTG1,
- Achilles Tendinopathy: MMP3

- Adams-Oliver syndrome: ARHGAP31, RBPJ, DOCK6, EOGT
- Adenylosuccinate Lyase Deficiency ADSL
- Aerobic Capacity: PPARGC1A
- AGPAT2
- AKT2
- Alcohol flush: ALDH2
- Alpers-Huttenlocher syndrome
- Alpha-1-Antitrypsin Gene (Serpina1 gene) CPT 81332
- Alpha (HBA1 HBA2) and Beta Thalassemia (HBB)
- Alport gene testing
- Ambry's PCDNext panel ARMC4, CCDC39, CCDC40, CCDC103, CCDC114, CFTR, DNAAF1, DNAAF2, DNAAF3, DNAAF5, DNAH5, DNAH11, DNAI1, DNAI2, LRRC6, OFD1, RPGR, RSPH4A, RSPH9, SPAG1, NME8 (TXNDC3)- 81222, 81223, 81479 6/14/16
- Amyotrophic lateral sclerosis (ALS, Lou Gehrig's disease) (**S3800**);
- Ambry's Cystic Fibrosis 508 First and reflex testing if negative to Cystic Fibrosis Full Gene Sequencing Analysis;
- Anemias not otherwise addressed,
- Angelman syndrome (AS) is a neuro-genetic disorder characterized by intellectual and developmental delay, sleep disturbance, seizures, jerky movements especially hand-flapping, frequent laughter or smiling, and usually a happy demeanor;
- Angelman-Like Syndromes CNTNAP2, SCL9A6, NRXN1, TCF4, UBE3A
- Angiotensin gene (CardiaRisk AGT)
- Antley-Bixler syndrome
- Antley-Bixler syndrome with genital anomalies and disordered steroidogenesis
- Apelin
- APOE (Apolipoprotein E)for CV disease and Alzheimer's Disease **(S3852)**
- ARHGEF9
- Array based comparative genome hybridization (Array CGH) in identification of the etiology of mental retardation, autism and developmental delay for any indications including cardiac defects, mental retardation, developmental delay, etc. but approved ONLY for testing on a product of conception (abortus tissue) **Except when meets criteria below;**
- Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C)

- ASS1 and SLC25A13 mutations of genes causing citrullinemia;
- Ataxia telangiectasia.
- ATN1
- ATP7B gene (Wilson disease)
- Autosomal Dominant Nocturnal Frontal Lobe Epilepsy CHRNA4, CHRNB2, CHRNA2
- Autosomal Dominant Partial Epilepsy with Auditory Features LGI1
- Baltic Myoclonus (Unverricht-Lundbord Disease) CSTB
- Beckwith Wiedemann Syndrome (including, but not limited to, genes KCNQ1OT1 (also known as LIT1), CDKN1C, H19)
- Benign Familial Neonatal-Infantile Seizures (Bfnis) SCN2A
- Benign Familial Neonatal Seizures (Bfns)KCNQ2, KCNQ3
- Bernard-Soulier Syndrome Gene
- Betaglobulin
- Biotinidase deficiency
- Birt-Hogg-Dubé syndrome - caused by mutations in the FLCN gene also known as folliculin;
- Bitter Taste: TAS2R38
- Blood Pressure Response to Exercise: EDN1
- BMI Response to Exercise: FTO
- Bone Marrow Failure Syndrome
- Brugada syndrome (**S3861**);
- BSCL2
- C3 Glomerulonephritis Sequencing Panel; CFH, C3, CFB, CFHR5, CFI, MCP (CPT 81479) 6/14/16
- CAPS, Cryopyrin-associated Period Syndrome, NLRP3
- Cardiomyopathy panel testing (e.g. Gene Dx Comprehensive Cardiomyopathy Panel; genes: ABCC9 , ACTC (ACTC1), ACTN2, ANKRD1, BAG3 , BRAF, CAV3, CRYAB , CSRP3, DES, DMD, DSC2, DSG2, DSP, DTNA, EMD, FKTN, GATAD1, GLA, HRAS, ILK, JPH2, JUP, KRAS, LAMA4, LAMP2, LDB3 (ZASP), LMNA, MAP2K1, MAP2K2, MTND1, MTND5, MTND6, MTTD, MTTG, MTTH, MTTI, MTTK, MTTL1, MTTL2, MTTM, MTTQ, MTTS1, MTTS2, MYBPC3, MYH7, MYL2, MYL3, MYLK2, MYOZ2, MYPN, NEBL , NEXN, NRAS, PDLIM3, PKP2, PLN, PRKAG2, PTPN11, RAF1, RBM20, RYR2, SCN5A, SGCD, SOS1, TAZ, TCAP, TMEM43, TMPO, TNNC1, TNNI3, TNNT2, TPM1, TTN, TTR, VCL)
- Carnitine SLC 22A5 Gene Test. SLC25A20 Gene And CPT11 Deficiency
- Catecholaminergic Polymorphic Ventricular Tachycardia - RYR2 and CASQ2 Genes;

- CAV1
- CCDC50,
- CHD7
- CD25 (IL2RA)
- CDH23,
- CFTR Full Gene Sequencing (**81223**)
- Charcot Marie Tooth gene test (**81324, 81325, 81326**);
- Choroidal neovascularization (e.g., Retnagene),
- Chromosome 4 Deletion Gene
- Chromosome 9 polymorphism 9p21 gene
- Chronic progressive external ophthalmoparesis (CPEO),
- CIDEC
- Circulating microRNAs (e.g., miR-1, miR-16, miR-26a, miR-27a, and miR-29a, miR-133a, and miR-199a-5p; not an all-inclusive list)
    - Oncology (thyroid), microRNA profiling by RT-PCR of 10 microRNA sequences, utilizing fine needle aspirate, algorithm reported as a positive or negative result for moderate to high risk of malignancy
    - Oncology (colorectal), microRNA, RT-PCR expression profiling of miR-31-3p, formalin-fixed paraffin-embedded tissue, algorithm reported as an expression score
    - MLH1 (mutL homolog 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
    - MSH2 (mutS homolog 2) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
    - MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
    - PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
    - Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure)
- Clarava™
- CLDN14,
- COCH,
- Coffin Lowry syndrome (RPS6KA3)

- Coffin Siris syndrome (ARID1A, ARID1B, SMARCA4, SMARCB1, and SMARCE1)
- COL7A Gene,
- Combimatrx's CombiSNP reflex FMR2 escalation testing
- Connective Tissue Disorders: Sequencing Panel which includes ACTA2, ACVR1, ADAMTS2, ATP6V0A2, CBS, CHST14, COL11A1, COL1A1, COL1A2, COL2A1, COL3A1, COL5A1,COL5A2, ELN, FBLN5, FBN1, FBN2, FKBP14, MYLK, NOTCH1, PKD2, PLOD1, PRDM5, SLC2A10, SLC39A13,SMAD3, TGFBR1, TGFBR2, ZNF469
- Courtagen genetic panels devACT neurodevelopmental panel, devSEEK neurodevelopmental panel, lysoSEEK lysosomal disorder panel, epiSEEK Comprehensive epilepsy panel, epiSEEK focus epilepsy panel, mtSEEK comprehenseive nuclear mitochondrial panel, and nucSEEK focus nuclear mitochondrial gene panel
- Connexin 30(GJB6 gene) is not medically necessary
- Congenital cataract gene test, is not medically necessary;
- Connective Tissue Disorders: Sequencing Panel which includes ACTA2, ACVR1, ADAMTS2, ATP6V0A2, CBS, CHST14, COL11A1, COL1A1, COL1A2, COL2A1, COL3A1, COL5A1,COL5A2, ELN, FBLN5, FBN1, FBN2, FKBP14, MYLK, NOTCH1, PKD2, PLOD1, PRDM5, SLC2A10, SLC39A13,SMAD3, TGFBR1, TGFBR2, ZNF469
- Coronary artery disease (e.g., the Corus CAD gene expression test);
- Craniosynostosis gene test
- Creatine Deficiency Syndromes GAMT, GATM
- CRYM
- CTLA4
- Cytochrome P450 OxidoReductase (POR) Deficiency with Disordered Steriodogenesis
- Cytogenomic constitutional (genome-hyphenwide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities [not covered for cardiovascular disease risk]
- DAX-1 gene is not medically necessary;
- deCODE AF, is not medically necessary;
- deCODE MI, is not medically necessary;
- deCODE T2 is not medically necessary;
- DFNA5,
- Diabetes type 2: CDKAL1, CDKN2B, ESR1, FTO, HHEX, HNF1B, IGF2BP2, JAZF1, KCNJ11, KCNQ1, MTNR1B, NOTCH2, PPARG, SLC30A8, TCF7L2, WFS1
- DIAPH1,

- DiGeorge Syndrome gene (also known as 22q11.2 deletion syndrome, Velocardiofacia syndrome, Familial third and fourth pharyngeal pouch syndrome, Sedlackova syndrome, and Thymic aplasia syndrome) is not medically necessary
- Dilated cardiomyopathy individual mutations and ALL panels ANKRD1, DMD, GATAD1, LDB3, LMNA, MYBPC3, MYH7, RBM20, SCN5A, TNNI3, TNNT2, and TTN
- Disordered steroidogenesis due to cytochrome p450 oxidoreductase deficiency
- DOCK8 deficiency
- DSPP,
- Dystonia gene testing is not medically necessary
- Early-Onset Epileptic Encephalopathy and/or Infantile Spasms ALDH7A1, ARX, ATP6AP2, CDKL5, PCDH19, POLG, PNPO, SCN1A, SLC2A1, SLC25A22, SPTAN1, STXBP1;
- Eating disinhibition: TAS2R38
- EGR2,
- ELANE gene
- Ellis-van Creveld syndrome (EVC, EVC2)
- Epidermolysis bullosa genetic testing including but not limited to genes CD151, CDSN, CHST8, COL17A1, COL7A1, DSP, DST, EXPH5, FERMT1, ITGA3, ITGA6, ITGB4, JUP, KRT14, KRT5, LAMA3, LAMB3, LAMC2, PKP1, PLEC, TGM5
- Endurance training: LIPC, PLP, PPARD
- ENG, ACVRL1 (ALK1), RASA1, and/or SMAD4 genes and associated panel for Hereditary Hemorrhagic Telangectasias;
- Epidermodysplasia Verruciformis (associated genes TMC6 & TMC8)
- Epidermolytic hyperkatosis,
- (Generalized) Epilepsy with Febrile Seizures Plus (GEFS+) GABRG2, SCN1A, SCN1B, SCN2A
- Epilepsy Advanced Sequencing Evaluation - Epileptic Encephalopathies
- Epilepsy with Variable Learning and Behavioral Disorders SYN1;
- Epilepsy and Seizure Disorder Panels including, but not limited to, the following genes: ABAT, ADSL, ALDH7A1, ARHGEF9, ARX, ASPM, ATP1A2, ATP6AP2, BCKDK, CACNA1A, CACNB4, CASK, CASR, CDKL5, CENPJ, CHRNA2, CHRNA4, CHRNB2, CLN3, CLN5, CLN6, CLN8, CNTNAP2, CPA6, CSTB, CTSD, CYP27A1, DCX, DNAJC5, EFHC1, EMX2, EPM2A, FLNA, FOLR1, FOXG1, GABRA1, GABRG2, GAMT, GATM, GOSR2, GPR56, GPR98,

GRIN2A, HCN1, HCN4, KCNA1, KCNJ10, KCNJ11, KCNMA1, KCNQ2, KCNQ3, KCNT1, KCTD7, LGI1, LIAS, MAGI2, MBD5, MCPH1, MECP2, MEF2C, MFSD8, MTHFR, NDE1, NDUFA1, NHLRC1, NRXN1, OPHN1, PAFAH1B1, PCDH19, PHF6, PLCB1, PNKP, PNPO, POLG, PPT1, PRICKLE1, PRICKLE2, PRRT2, RELN, SCARB2, SCN1A, SCN1B, SCN2A, SCN3A, SCN8A, SCN9A, SHH, SIX3, SLC19A3, SLC25A19, SLC25A22, SLC2A1, SLC9A6, SPTAN1, SRPX2, ST3GAL3, ST3GAL5, STIL, STXBP1, SYN1, TBC1D24, TCF4, TPP1, TSC1, TSC2, TSEN54, UBE3A, WDR62, ZEB2 (e.g., Emory University's Epilepsy and Seizure Disorders: Sequencing Panel, Ambry EpiFirst – Focal, EpiNext)

- ESPN,
- ESRRB,
- EXT1 and/or EXT2 genes for Hereditary Multiple Osteochondromatosis (also known as Hereditary Multiple Exostoses)
- EYA4,
- Factor H gene or complement factor H, CFH gene;
- Familial cold urticaria/familial cold autoinflammatory syndrome, FCAS
- Familial Congenital Cavernous Malformations (FCCM),
- Fascioscapulohumeral Muscular Dystrophy (FSHD)
- Fatty Acid Oxidation Panel for Glutaric Aciduria Type 2 is considered investigational and experimental and not medically necessary;
- FBN1 is a large gene used in association with Marfan Syndrome, isolated ectopia lentis, autosomal dominant Weill-Marchesani syndrome, MASS syndrome, and Shprintzen-Goldberg craniosynostosis syndrome. It is the main protein of a group of connective tissue microfibrils that is essential to normal elastic fibrillogenesis;
- FBN 2 gene test is not medically necessary;
- Fever Mutation Panel
- FGFR2
- FGFR3 mutation Achondroplasia(Dwarfism)
- FMR2
- Food desire: ANKK1/DRD2
- FOXP3
- Familial Hyperinsulinism: ABCC8, KCNJ11, GLUD1, GCK, HADH, HNF1A, HNF4A, SLC16A1, and UCP2
- G6PC (glucose-6-phosphatase, catalytic subunit)
- G6PC3
- G6PD (for pharmacogenetic, see genetic testing 34 E)
- Galactosemia gene is not medically necessary;

- GDAP1,
- GeneDx Arrhythmia panel AKAP9, ANK2, CACNA1C, CACNB2, CASQ2, CAV3, DSC2, DSG2, DSP, GPD1L, HCN4, JUP, KCNE1, KCNE2, KCNE3, KCNH2, KCNJ2, KCNJ5, KCNJ8, KCNQ1, NKX2.5 , PKP2, RANGRF, RYR2, SCN1B, SCN3B, SCN4B, SCN5A, SNTA1, TMEM43
- GeneDx Combined Cardiac panel ABCC9 , ACTC (ACTC1), ACTN2, AKAP9, ANK2, ANKRD1, BAG3 , BRAF, CACNA1C, CACNB2, CASQ2, CAV3, CRYAB , CSRP3, DES, DMD, DSC2, DSG2, DSP, DTNA, EMD, FKTN, GATAD1, GLA, GPD1L, HCN4, HRAS, ILK, JPH2, JUP, KCNE1, KCNE2, KCNE3, KCNH2, KCNJ2, KCNJ5, KCNJ8, KCNQ1, KRAS, LAMA4, LAMP2, LDB3 (ZASP), LMNA, MAP2K1, MAP2K2, MTND1, MTND5, MTND6, MTTD, MTTG, MTTH, MTTI, MTTK, MTTL1, MTTL2, MTTM, MTTQ, MTTS1, MTTS2, MYBPC3, MYH7, MYL2, MYL3, MYLK2, MYOZ2, MYPN, NEBL , NEXN, NKX2.5 , NRAS, PDLIM3, PKP2, PLN, PRKAG2, PTPN11, RAF1, RANGRF, RBM20, RYR2, SCN1B, SCN3B, SCN4B, SCN5A, SGCD, SNTA1, SOS1, TAZ, TCAP, TMEM43, TMPO, TNNC1, TNNI3, TNNT2, TPM1, TTN, TTR, VCL
- Genetic risk for decreased HCL cholesterol: ABCA1, ANGPTL4, CETP, FADS1, GALNTZ, HNF4A, KCTD10, LCAT, LIPC, LIPG, LPL, PLTP, TTC398, ZNF259
- Genetic risk for elevated LDL cholesterol: ABCG8, APOB, CELSR2, HMGCR, HNF1A, Intergenic, LDLR, MAFB, NCAN, PCSK9
- Genetic risk for elevated trigylcerides: ANGPTL3, APOB, FADS1, GCKR, LPL, MLXIPL, NCAN, PLTP, TRIB1, XKR6, ZNF259
- Genetic risk due to decreased vitamin B2: MTHFR
- Genetic risk for decreased folate: MTHFR
- Genetic risk for decreased vitamin A: BCMO1
- Genetic risk for decreased vitamin B12: FUT2
- Genetic risk for decreased vitamin B6: NBPF3
- Genetic risk for decreased vitamin C: SLC23A1
- Genetic risk for decreased vitamin D: GC
- Genetic risk for increased vitamin E: Intergenic
- Genetic risk for decreased adiponectin: ADIPOQ
- Genetic risk for decreased omega-6 and omega-3: FADS1
- GFI1
- GIPC3,
- GJB1,
- GJB2 (Connexin 26) Gene mutation is not medically necessary;
- GJB3,

- Glaucoma Genetic Testing
- GLIS2/NPHP7 gene sequencing is not medically necessary;
- Glucose transporter Type I Deficiency Syndrome SLC2A1
- Glutaric Aciduria 11
- GNAS Gene for pseudohypoparathyroidism,
- GPR56 gene for polymicrogyria
- GPSM2,
- GRHL2,
- GRIN2A
- Growth stimulation expressed gene 2 (ST2, Interleukin 1 receptor like-1)
- GRXCR1
- HAX1
- HDL Cholesterol response to exercise: PPARD
- Hemiplegic migraine (HM),
- Hemiplegic Migraine Panel(CACNA1A, ATP1A2,PRRT, SCN1A)
- Hepatocerebral mtDNA Depletion Panel
- Hereditary cardiomyopathies are **investigational and not medically necessary** including but not limited to, arrhythmogenic right ventricular dysplasia/dilated, restrictive, and left ventricular noncompaction cardiomyopathies;
- Hereditary Hemorrhagic Telangiectasias; (BMP9, SMAD4, ENG, ACVRL1, RASA1)
- Hereditary pancreatitis (PRSS1)
- Hereditary Retinal Disorders Genetic Panel Lab Test
- Hereditary sensory and autonomic neuropathies genetic testing
- Hereditary Spastic Paraplegia
- Hereditary spherocytosis and elliptocytosis
- HFPL5,
- HGF,
- HNPP associated with hereditary neuropathy/palsies aka Tomaculous Neuropathy 17p11.2 microdeletion
- Hunger: NMB
- Hunter syndrome
- Hyperhomocysteinemia - MTHFR Gene
- Hyperimmuneoglobulin D Syndrome, HIDS, MVK mutation
- Hypokalemic Periodic Paralysis
- Hypohidrotic Ectodermal Dysplasia Gene
- Idiopathic Progressive Polyneuropathy Gene,
- ILDR1
- Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not

otherwise specified [adiponectin] [leptin] [interleukin-hyphen6 (IL-hyphen6)] [tumor necrosis factor alpha (TNF-hyphena)] [Oxidized phospholipids] [interleukin 17] [toll-hyphenlike receptor 4 (TLR4)] [Interleukin-hyphen18 (IL-hyphen18)] [soluble cell adhesion molecules (e.g., intercellular adhesion molecule-hyphen1 [ICAM-hyphen1], vascular cell adhesion molecule-hyphen1 [VCAM-hyphen1], E-hyphenselectin, P-hyphenselectin)] [transforming growth factor beta]

- Impulse Control, ADHD, Oppositional Defiance Disorder Gene;
- Incontinentia Pigmenti
- Inherigen Plus which includes ACTA2, CBS, COL3A1, FBN1, FBN2, MYH11, SLC2A10, SMAD3, TGFBR1, TGFBR2
- Inheritest
- Insulin sensitivity response to exercise: LIPC
- Interleukin 6 (IL-6)
- Invitae Alternating Hemiplegia of Childhood Panel (genes ATP1A2 and ATP1A3)
- Isovaleric Acidemia
- Jaundice Chip array is not medically necessary
- JAG1 testing for Alagille Syndrome
- Juvenile Myoclonic Epilepsy (JME) CACNB4, EFHC1, GABRA1
- Kabuki Syndrome Gene
- KBG Syndrome (ANKRD11 Gene)
- KCNC2 or KCNC3
- KCNQ4
- KCNT1
- Kinesin-like protein 6 (KLP6)
- Klippel-Feil syndrome
- L1CAM gene laboratory test (Rare Disorders Genetic Test)
- Lafora Disease EPM2A, EPM2B
- Leber's hereditary optic neuropathy is not medically necessary and the diagnosis is not going to change the outcome
- Legius Syndrome
- LEMD3
- Leopard syndrome (PTPN11, RAF1 genes)
- Leptin 84100
- Lesch-Nyhan Syndrome - HPRT1 Gene;
- Liddle syndrome (genes SCNN1B, SCNN1G, BESC1, or BESC3)
- Lissencephaly (all genes)
- LITAF,

- Low Bone Mass Panel for Osteoporosis including genes ALPL, B4GALT7, COL1A1, COL1A2, COL3A1, COL5A1, COL5A2, CRTAP, FBN1, FKBP10, IFITM5, LEPRE1, PLOD2, PLOD3, PPIB, SERPINF1, SLC34A1, SLC39A13, SLC9A3R1, SP7, TNFRSF11A, TNFRSF11B and WNT1
- LMNA
- LMX1B Gene Testing (Nail-Patella Syndrome)
- Loeys-Dietz syndrome 1 (TGFBR1) or 2 (TGFBR2);
- LOXHD1,
- LRTOMT,
- Mannose Binding Lectin
- MARVELD2,
- Matching diet type: ADIPOQ, APOA2, FTO, KCTD10, LIPC, MMAB, PPARG
- Maturity Onset Diabetes of Youth (MODY)
- MC4R
- McCune-Albright syndrome
- Metabolism: LEPR
- Metachromatic leukodystrophy (MLD)
- Microcephaly with Early-Onset Intractable Seizures and Developmental Delay (MCSZ) PNKP
- MID1 genetic testing (Opitz G / BBB)
- Menopause Karotype
- MECP2 gene for Rett syndrome (81302, 81303 & 81304);
- Medium Chain Acyl-coA Dehydrogenase Deficiency (MCADD)
- MELAS (mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes) (MTTL1, tRNAleu);
- MFN2,
- Microdeletion Syndromes on Chromosome 1-11 including but not limited to the following: 1q21, HYDIN, GJA5, GJA8, TAR syndrome (RBM8A), 2p15-16 (XPO1 and OTX1) 2q23.1 Smith-Magenis syndrome. (MBD5 and MECP2) 2q37 Syndrome (HDAC4) 3p SYNDROME CNTN4 (contactin 4), 3q29 SYNDROME (PAK3 and DPG2) 4p SYNDROME (WOLF-HIRSCHHORN SYNDROME) WHSCR1 and WHSCR2, 5q35 SYNDROME (SOTOS SYNDROME) NSD1 and NKX2.5 6p25 SYNDROME FKHL7 FOXC1, FOXF2, and FOXQ1 7q11.23 (WILLIAMS SYNDROME) elastin gene ELN 8q22.1 SYNDROME (NABLUS MASK-LIKE FACIAL SYNDROME) 8q24.11 SYNDROME (LANGER-GIEDION SYNDROME OR TRICHORHINOPHALANGEAL SYNDROME TYPE II) TRPS1 9p22 SYNDROME 9q34.3 SYNDROME OR 9q SUBTELOMERE SYNDROME EHMT1 10p14-p13 (DiGEORGE SYNDROME TYPE II) GATA3 11p13 SYNDROME (WAGR SYNDROME) PAX6 and WT1

11p11.2 SYNDROME (POTOCKI-SHAFFER SYNDROME) EXT2 11q24.1 SYNDROME (JACOBSEN SYNDROME) ETS-1, FLI-1, NFRKB, and JAM3, KCNJ1 and ADAMTS15

- Migrainous vertigo,
- miR-96,
- miR-182,
- miR-183,
- Mitochondrial Disorder gene testing
- Mosaic Down Syndrome Gene,
- Mowat-Wilson Syndrome ZEB2
- MPZ,
- MT-RNR1,
- MT-TS1 Gene,
- Muckle Wells syndrome NLRP3
- Mucopolysaccharidosis (MPS) genetic testing
- MYH8 Gene(Trismus-pseudocamptodactyly syndrome)
- MYH9,
- MYH14,
- MYO1A,
- MYO3A,
- MYO6,
- MYO7A,
- MYO15A,
- Myoclonus-dystonia (epsilon-sarcoglycan gene (SCGE) deletion analysis);
- NEFL,
- Neimann Pick Disease;
- Neonatal Onset Multisystemic Inflammatory Disorder, NOMID, NLRP3
- Neuronal Ceroid Lipofuscinoses (NCL)CLN3,CLN5,CLN6,CTSD,CLN8,MFSD8, PPT1,TPP1
- Congenital Neutropenia Panel
- NLRP3 testing for Muckle Wells syndrome is not medically necessary;
- Noonan syndrome
- NOTCH2 testing for Alagille Syndrome
- NPHS2, LAMB2 and FSGS Genetic Testing for Nephrotic Syndrome
- NSD1 for Soto syndrome;
- Nuclear encoded mitochondrial genomic sequencing panels (eg, Nuclear-Mito NGS Panel)
- Obesity: FTO, MC4R
- OCA 2 p gene deletion analysis mutations in OCA2 result in type 2 oculocutaneous albinism. Oculocutaneous albinism consists of a group of at least 10 different inherited skin

diseases characterized by a generalized decrease of pigmentation in the skin, eyes, and hair because of abnormal melanocyte function;
- Oculopharyngeal muscular dystrophy is not medically necessary
- Ohtahara Syndrome STXBP1, ARX
- OPA 1 Gene
- Osteoarthritis: GDF5, PTGS2
- Osteogenesis imperfecta
- Osteoprotegerin
- OTOA
- OTOF
- Microarray and multi-gene panels for nonsyndromic hereditary hearing loss (e,g,, OtoScope, OtoGenome, etc.) (81430, 81431)
- Pallister-Hall syndrome GL13 gene
- Paragangliomas Pheochromocytoma Syndromes, Hereditary - SDHB, SDHC, and SDHD Genes;
- Parkinson's
- PAX2 Gene,
- PCDH15
- PDGFR (Platelet Derived growth Factor Receptor),
- Pelizaeus Merzbacher gene
- Periodic fever syndrome panel,
- PEX6
- Pfeiffer syndrome
- Phox2b Gene
- PLIN1
- PJVK,
- PMP22,
- POLG (**POL**ymerase **G**amma Gene)
- Polycystic kidney disease (all types of PKD and genetic tests including ADPKD and ARPKD)
- Pompe gene testing,
- Pontocerebellar hypoplasia genetic testing including, but not limited to the following genes: CASK, OPHN1, RARS2, TSEN2, TSEN34, TSEN54, VRK1, EXOSC8
- POU4F3,
- PPARG
- Prader–Willi Syndrome gene testing (SNRPN/UBE3A);
- PreDx Diabetes Risk Test;
- Primary dystonia;
- Progressive cerebellar ataxia gene testing;
- Progressive Myoclonic Epilepsy (PME) CLN3, CLN5, CLN6, CLN8, CSTB, CTSD, EPM2A, MFSD8, NHLRC1, PPT1,

PRICKLE1, TPP1

- PROMETHEUS® Lacto*TYPE*®Lactose intolerance genetics test to help identify primary lactase non-persistence,
- PRPS1,
- PRX
- PTRF
- Pulmonary Alveolar Proteinosis next generation sequencing or mutation testing on genes ABCA3, CSF2RA, CSF2RB, FOXF1, NKX2-1, SFTPB, SFTPC, and/or SLC7A7
- TPRQ,
- Pyridoxine Dependent Seizure ALDH7A1
- RAI1 gene
- RB1Gene
- RDX
- Resistin
- Response to monounsaturated fats: ADIPOQ, PPARG
- Response to polyunsaturated fats: PPARG
- Retinol binding protein 4 (RBP4)
- Rh C and Rh D genotyping;
- Repeat/Duplicative genetic testing
- Retinitis Pigmentosa genetic testing
- Rett/Atypical Rett Syndrome CDKL5, FOXG1, MECP2 (81302, 81303 & 81304);
- Myopathy/Rhabdomyolysis panel including the genes ACADL, ACADM, ACADVL, ACAD9, AGL, C10orf2, CPT1B, CPT2, GAA, GYS1, HADHA, HADHB, LPIN, OPA1, OPA3, PFKM, PGAM2, PGM1, PHKA1, POLG, POLG2, PYGM, RRM2B, SLC22A5/OCTN2, SUCLA2, TK2, TYMP
- RNASEH2A
- RNASEH2B
- RNASEH2C
- SAMHD1
- Satiety: FTO
- Schizencephaly;
- SCN1A for Dravet Syndrome;
- SCN4A Gene
- SCN8A
- SCN9A
- Scoliscore test to evaluate the risk of progression of Idiopathic scoliosis in immature children;
- SALL4 Gene Analysis for Duane-Radial Ray syndrome / Acro-Renal-Ocular syndrome
- Secretory Type II Phospholipase A2 (Spla2-IIA)
- Selective Serotonin Reuptake Inhibitors (SSRIs) - Cytochrome P450 Polymorphism Testing ;

- Septo-Optic Dysplasia (SOD) - Genetic Testing (HESX1)
- SERPINC1
- Short Stature Homeobox (SHOX) gene testing
- Shwachman-Diamond syndrome (SBDS gene)
- Sickle Cell,
- SLC17A3,
- SLC26A4 gene “Solute carrier family 26, member 4” for Pendred syndrome,
- SLC26A5,
- SLC37A4
- SLC9A6
- Sleep-walking
- Snacking: LEPR
- SPINK1 gene
- SPRED1 (sprout-related, EVH1 domain containing 1) (eg, Legius syndrome)
- STAT 3 for hyper IgE syndrome
- STAT5
- Stickler Syndrome COL2AI Gene, COL11A1 and COL11A2
- STRC,
- Strength Training: INSIG2
- Sweet tooth: SLC2A2
- SYNGAP1
- TBC1D4
- TECTA,
- TGFBR1 and TGFBR2 gene testing and/or Marfan *Panel* containing other associated mutations if ordered because FBN1 testing is negative
- TJP2,
- TMC1,
- TMIE,
- TMPRSS3,
- TRAPS, Tumor Necrosis Factor Receptor-associated Periodic Syndrome, TNFRSF1A, or TNFR1
- TPRN,
- TREX1
- TRIOBP,
- TTR (Transthyretin) Gene
- Trismus Pseudocamptodactyly Syndrome
- Tuberous Sclerosis testing (TSC2 Gene)
- Tuteva™
- X chromosome activation status testing
- Uniparental Disomy
- Venous thrombosis: MTHFR
- Very Long Chain Acyl-CoA Dehydrogenase (VLCAD)

Deficiency
- VICI Syndrome (EPG5 Gene)
- Visfatin
- Waardenburg Syndrome
- Weight loss-regain: ADIPOQ
- West Syndrome ARX, CDKL5, STXBP1,TSC1,TSC2;
- WFS1
- Whole Exome Sequencing (WES)
- Exome Sequence Analysis (CPT 81415, 81416, 81417)
- Whole Genome Sequencing (WGS)
- Genome Sequence Analysis (CPT 81425, 81426, 81427)
- xTAG Gastrointestinal Pathogen Panel
- ZMPSTE24
- Any other test not listed below as covered is considered among those that are not medically necessary.

The following are considered Not Medically Necessary:

- Ehlers-Danlos Syndrome can be diagnosed with a skin biopsy.

Authorization: Pre-certification by the Plan is required.

Autosomal recessive: A genetic condition that appears only in individuals who have received two copies of an autosomal gene, one copy from each parent. The gene is on an autosome, a nonsex chromosome. The parents are carriers who have only one copy of the gene and do not exhibit the trait because the gene is recessive to its normal counterpart gene

X-linked recessive inheritance - hereditary pattern in which a recessive gene on the X chromosome results in the manifestation of characteristics in male offspring and a carrier state in female offspring

Procedure:

Genetic Testing is considered medically necessary for the prevention, diagnosis and treatment of patients who meet **ALL** of the following:

1. There is sufficient Published Scientific Evidence or 3rd party Consensus in the Medical Community that the results of the specific genetic Testing improves clinical outcomes.

OR

2. There is an approved mutation specific treatment available

AND

3. There is sufficient scientific evidence that the results of the genetic test could impact the medical management of the patient with a resulting improvement in health outcomes;

AND

4. The genetic disorder is associated with a potentially significant disability or has a lethal natural history;

AND

5. The results of the genetic test could impact the medical management of the individual;

AND

6. After completion of a thorough history, physical examination, pedigree analysis, genetic counseling, relevant diagnostic and biochemical tests (if any), the patient meets criteria for any of the following approved tests:

(**Criteria are listed individually for each test below**)

a. CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy)
b. Cystic Fibrosis
c. Fragile X
d. Long QT Genetic Testing
e. Muscular Dystrophy and Spinal Muscular Atrophy(SMA)
    1. Congenital Muscular Dystrophy
    2. Duchene Muscular Dystrophy (DMD),
    3. Emery-Dreifuss Muscular Dystrophy (EDMD1, 2, and 3)(FGFR2)
    4. Familial Myotonic Dystrophy, (FMD)
    5. Fascioscapulohumeral Muscular Dystrophy (FSHD) FSHMD1A) (FGFR3)
    6. Limb girdle Muscular Dystrophy (LGMD1, LGMD2) (FKRP (Fukutin related protein))
    7. Ullrich Muscular Dystrophy COL6A2

f. Karyotype (cytogenetic analysis)
g. Fanconi Testing (FANC)
h. Retinoblastoma
i. Familial HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS
j. Other Miscellaneous Disorders
    1. Bloom syndrome, BLM Gene
    2. Canavan disease, ASPA Gene
    3. Deficiency, Familial hyperinsulinism,
    4. Dihydrolipoamide dehydrogenase
    5. Dysautonomia (Riley-Day syndrome),
    6. Fanconi anemia FANC Genes
    7. Gaucher's disease,
    8. Glycogen storage disease type 1 G6PC and SLC37A4 Genes

9. Huntington Disease (HTT gene)
10. Inheritest Universal screening
11. Maple syrup urine disease BCKDHA, BCKDHB, and DBT Genes
12 Mucolipidosis IV, MCOLN1 Gene
13 Nemaline myopathy,
14. Nieman Pick Disease Type A, SMPD1, NPC1, and NPC2 Genes
15. Usher syndrome type 1F or Usher syndrome type 3,

k. Marfan syndrome
l. CGH Array or SNP Microarray (single nucleotide polymorphism)
m. Neurofibromatosis 1 (NF1) and 2 (NF2)
n. Familial Hypercholesterolemia
o. Familial Mediterranean Fever (FMF)
p. Ashkenazi Jewish Genetic panel
q. Spinal Muscular Atrophy (SMA)
r. Hypertrophic cardiomyopathy (HCM)
s. Mucopolysaccharidosis IVA (Morquio syndrome)
t. CD40 Ligand Deficiency (CD40LG or X-Linked Hyper IgM) genetic testing
u. Hereditary Fructose Intolerance Testing (ALDOB Gene)
v. Tay-Sach's disease, HEXA Gene
w Wiskott-Aldrich syndrome (WAS) gene mutation testing
x. Phenylalanine hydroxylase (PAH) Testing for phenylketonuria (PKU)
y. Envisia Idiopathic Pulmonary Fibrosis Diagnostic testing
z. McKusick-Kaufman Syndrome Single Gene Test

A. **CADASIL**

CADASIL (cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy) is the most common form of hereditary stroke disorder, and is thought to be caused by mutations of the Notch 3 gene on chromosome 19. The most common clinical manifestations are migraine headaches and transient ischemic attacks or strokes, which usually occur between 40 and 50 years of age,

Clinical Indications:
DNA testing for CADASIL for **ONE** of the following indications **if ordered by a geneticist:**

1. Symptomatic members younger than 60 years of age with a family history consistent with an autosomal dominant pattern of inheritance of this condition; **OR**
2. Pre-symptomatic individuals younger than 60 years of age with a family history consistent with an autosomal dominant pattern of inheritance and a known mutation in an affected member of the family.

B. **Cystic Fibrosis for Carrier Testing**

Cystic Fibrosis (CF) is an inherited disease that causes thick, sticky mucus to build up in the lungs and digestive tract. It is one of the most common chronic lung diseases in children and young adults, and may result in early death.

Clinical Indications:
The Plan covers requests for common mutations included in CPT codes **81221** (familial variants) or **81220** (common variants) endorsed by the American College of Medical Genetics (ACMG) for Cystic Fibrosis testing.No precertification is required. (**See criteria below for extended and full CF gene sequencing (CPT codes 81222 - 81224).)**

Additional testing (eg. HerediT CF carrier testing)

Extended CFTR mutation panels (**Code 81222 and 81224**) are approved for patients meeting **ANY** of the following 3 criteria (but not full sequencing, see exclusions):

1. Individuals with reproductive partners with cystic fibrosis or congenital absence of the vas deferens and no identified mutation with standard gene sequencing,

OR

2. Individuals with a family history of cystic fibrosis with no identified mutation on basic/standard gene sequencing,

OR

3. Individuals with elevated or indeterminate sweat chloride levels where from zero to up to 2 mutations have been identified by basic/standard gene sequencing.

Full CFTR sequencing (81223) is NOT covered for ANY indication, (see in exclusions above)

C. **Fragile X**

Fragile X includes: (FXS), the most common cause of inherited mental impairment. This impairment can range from learning disabilities to more severe cognitive or intellectual disabilities. (Sometimes **referred to** as mental retardation) FXS is the most common known cause of autism or "autistic-like" behaviors. Symptoms also can include characteristic physical and behavioral features and delays in speech and language development.

Fragile X syndrome is a family of **genetic conditions**, which can impact individuals and families in various ways. These genetic conditions are related in that they are all caused by gene changes in the same gene, called the FMR1 gene.

Clinical Indications: FMR1 (codes 81243 and 81244) covered on request.

D. **Long QT Genetic Testing** (KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2 genes)

Long QT Syndrome (LQTS) is a heart rhythm disorder that can potentially cause fast, chaotic heartbeats. These rapid heartbeats may trigger a sudden fainting spell or seizure.

Clinical Indications: Should meet **one** of the following:

1. For members with a prolonged QT interval on resting electrocardiogram (a corrected QT interval (QTc) of 450 msec without an identifiable external cause for QTc prolongation (such as heart failure, bradycardia, electrolyte imbalances, certain medications and other medical conditions);

OR

2. Persons with first-degree relatives (siblings, parents, offspring) with a known or suspected LQT mutation, or long QT syndrome.

E. **Muscular Dystrophy**

Several varieties of muscular dystrophy can be distinguished on clinical, genetic, morphologic, and physiologic grounds. The classification includes Duchenne and Becker muscular dystrophies, both X-linked disorders; facioscapulohumeral muscular dystrophy, which is autosomal dominant; and limb-girdle muscular dystrophy, generally autosomal recessive.

Clinical Indications:
Muscular Dystrophy genetic testing may be indicated when the appropriate clinical situation is present, as indicated by **1 or more** of the following:

1. The member has unexplained progressive muscle weakness, abnormal gait, or other clinical findings consistent with muscular dystrophy or spinal muscular atrophy. These findings may also include abnormal laboratory findings (e.g., elevated serum CK (creatine kinase), or a positive family history;

OR

2. The member has a confirmed diagnosis of muscular dystrophy and genetic testing is required to establish the disease-causing mutation;

Tests include ANY of the following:

1. Congenital Muscular Dystrophy including ANY of the following: ACTA1, AMPD1, AMPD3, CAPN3, CAV3, COL6A1, COL6A2, COL6A3, DES, DMD, DYSF, EMD, FKRP, FKTN, ITGA7, LAMA2, LARGE, LMNA, MYOT, NEB, PEX1, PEX12, PEX14, PEX2, PEX26, PEX3, PEX5, PEX6, PLEC, PMM2, POMGNT1, POMT1, POMT2, RYR1, RYR2, SEPN1, SGCA, SGCB, SGCD, SGCE, SGCG, SIL1, TCAP, TNNI2, TNNT1, TPM2, TPM3, TRIM32, TTN, ANO5
2. Duchene Muscular Dystrophy (DMD),
3. Emery-Dreifuss Muscular Dystrophy (EDMD1, 2, and 3)(FGFR2)
4. Familial Myotonic Dystrophy, (DMPK, DM2 (ZNF9), or CNBP))
5. Fascioscapulohumeral Muscular Dystrophy (FSHD) FSHMD1A) (FGFR3)
6. Limb girdle Muscular Dystrophy (LGMD1, LGMD2) (FKRP (Fukutin related protein))
7. Ullrich Muscular Dystrophy COL6A2

F. Karyotype (cytogenetic analysis)

Karyotypes describe the number of chromosomes, and what they look like under a light microscope- Along with 88289 Chromosome analysis; additional high resolution study and 88230 (Non-neoplastic Tissue Culture)

Clinical Indications: Covered without preauthorization (precertification).

G. Fanconi Testing (FANC))—(FANCC 81242 including DEB Chromosome Assay, 88248)

Fanconi anemia is characterized by diverse congenital malformations of multiple body systems including involvement of the skeletal system, eyes, kidneys and urinary tract, ears, heart, gastrointestinal system, and central nervous system. Patients develop progressive pancytopenia, and predisposition to both hematologic malignancies and solid tumors. The condition is associated with a mutation in one of at least 15 genes (collectively called FANC), which are responsible for the 15 known Fanconi anemia complementation groups. Fanconi anemia is diagnosed by performing cytogenetic testing in which increased chromosomal breakage or rearrangement is noted after DNA from peripheral blood is exposed to an interstrand cross-linking agent such as diepoxybutane or mitomycin C

Clinical Indications for genetic Testing for Fanconi Anemia include ANY of the following:

1. Patient of Ashkenazi Jewish ancestry and of reproductive age.

OR

2. Patient with family history of Fanconi anemia, and prior identification of disease-causing mutations in relatives;

OR

3. Prior to gamete donation if gamete recipient is carrier;

OR

4. Reproductive partner of FANC gene mutation carrier;

OR

5. Equivocal or indeterminate cytogenetic testing for chromosomal breakage or rearrangement in presence of DNA interstrand cross-linking agent (eg, diepoxybutane or mitomycin C);

OR

6. Identification of disease-causing mutation in patient with confirmed diagnosis

H. Retinoblastoma (RB1)

Retinoblastoma (RB1) Retinoblastoma is the most common intraocular cancer in children. It is a malignant tumor of the retina that occurs in young children, usually before the age of 5 years. Approximately 40% to 50% of retinoblastomas are classified as hereditary and are caused by mutations in the RB1 tumor suppressor gene, that's inherited in an autosomal dominant manner. Hereditary retinoblastoma is the result of a germline mutation followed by a somatic mutation in the RB1 gene.(1)(7) (EG 2) Sporadic (nonhereditary) retinoblastoma results from somatic mutations in both alleles of the RB1 gene

Clinical Indications:

RB1 gene testing may be indicated when **ALL** of the following are present:

1. Diagnosis or screening for hereditary retinoblastoma, as indicated by **1 or more** of the following:

    a. First-degree relative of patient with known RB1 mutation

    OR

    b. Patient with retinoblastoma, with or without family history of retinoblastoma

    OR

    c. Preimplantation genetic diagnosis for families in which disease-causing mutation has been identified;

    OR

d. Prenatal diagnosis for] pregnancies at increased risk when disease-causing allele of affected family member has been identified or linkage has been established in family;

AND

2. Testing is accompanied by genetic counseling.

I. Familial Hemophagocytic Lymphohistiocytosis: Covered if requested by name without criteria (there is no specific code)

J. Other Miscellaneous Disorders

Clinical Indications:
Testing will be covered for **ANY** of the following if requests meet **ANY** of the following appropriateness criteria:

1. Patient with positive family history or known mutation of the disease in the family,

OR

2. Reproductive partner of known gene mutation carrier,

OR

3. Equivocal or indeterminate diagnostic testing of a symptomatic individual,

OR

4. Need to establish disease-causing mutation in patient with confirmed diagnosis

The following Disorders are included in this area—

1. Bloom syndrome, BLM Gene
2. Canavan disease, ASPA Gene
3. Deficiency, Familial hyperinsulinism,
4. Dihydrolipoamide dehydrogenase
5. Dysautonomia (Riley-Day syndrome),
6. Fanconi anemia FANC Genes
7. Gaucher's disease,
8. Glycogen storage disease type 1 G6PC and SLC37A4 Genes
9. Huntington Disease (HTT gene)
10. Inheritest Universal screening
11. Maple syrup urine disease BCKDHA, BCKDHB, and DBT Genes
12. Mucolipidosis IV, MCOLN1 Gene

13. Nemaline myopathy,
14. Nieman Pick Disease Type A, SMPD1, NPC1, and NPC2 Genes
15. Usher syndrome type 1F or Usher syndrome type 3,

K. **Marfan syndrome-(FBN1 gene testing) for Marfan syndrome** FBN1 is a large gene used in association with Marfan Syndrome, isolated ectopia lentis, autosomal dominant Weill-Marchesani syndrome, MASS syndrome, and Shprintzen-Goldberg craniosynostosis syndrome. It is the main protein of a group of connective tissue microfibrils that is essential to normal elastic fibrillogenesis. See clinical indications for Marfan syndrome below FBN 2 gene test is not medically necessary.

Clinical Indications for Marfan syndrome:

1. Patient does not fulfill Ghent diagnostic criteria but has one major feature of Marfan syndrome

OR

2. Patient is a first-degree relative of an individual with known disease-causing variants

L. **CGH Array or SNP Microarray (single nucleotide polymorphism)** is considered medically necessary for patients **under the age of 13 (under age 21 for EPSDT)** and ANY of the following criteria below is met**:**

1. Patient has multiple anomalies not specific to a known genetic syndrome;

OR

2. Patient has apparently non-syndromic developmental delay or intellectual disability;

OR

3. Patient with Autism spectrum disorders.

M. **Neurofibromatosis 1 (NF1) and 2 (NF2)**

1. NF1 testing for 1 or more of the following:

   (a.) Diagnosis of neurofibromatosis type 1 uncertain after clinical evaluation and conventional diagnostic testing;

2. NF2 testing for 1 or more of the following:

   (a) Diagnosis of neurofibromatosis type 2 uncertain after clinical evaluation and conventional diagnostic testing;

OR

(b) Patient with bilateral vestibular schwannomas;

OR

(c) Patient with multiple spinal tumors (schwannomas, meningiomas, gliomas);

N. Familial Hypercholesterolemia

The following are clinical indications for homozygous familial hypercholesterolemia (HoFH) and heterozygous familial hypercholesterolemia (HeFH) (e.g., genetic testing of LDL receptor, ApoB, PCSK9, or autosomal recessive hypercholesterolemia adaptor protein gene locus).
Testing is considered medically necessary for requests meeting both of the following (1 and 2):

1. Either (a or b)

a. Plasma cholesterol level in an adult over the age of 18 greater than or equal to 310 mg/dL

OR

b. Plasma cholesterol level in a child (<18 y/o) greater than or equal to 230 mg/dL

AND

2. ANY ONE or MORE of the FOLLOWING (a-c):

a. **Family history of premature coronary heart disease** (men < 55 years of age, women < 60 years of age) **or sudden cardiac death** (an unexpected death due to cardiac causes that occurs in a short time period [generally within 1 hour of symptom onset]);

OR

b. Presence of **xanthomas** on physical Exam

OR

c. Known family history (first or second degree relative) with familial hypercholesterolemia and/or any of the associated mutations.

O. Familial Mediterranean Fever (FMF)

Diagnostic MEFV gene testing may be indicated when clinical findings or diagnostic testing are suggestive of familial Mediterranean fever, as indicated by **1 or more** of the following (1,2,3, or 4):

1. Amyloidosis (senile systemic type)

OR

2. Favorable response to colchicine therapy

OR

3. Recurrent episodes of fever associated with **2 or more** of the following:

    a) Acute abdominal pain with possible peritoneal signs
    b) Acute arthritis of ankle, knee, or hip
    c) Elevated erythrocyte sedimentation rate or C-reactive protein
    d) Elevated serum fibrinogen
    e) Erysipelas-like erythema of skin[C]
    f) Leukocytosis
    g) Pleuritis

OR

4. First-degree relative of individual with confirmed diagnosis of familial Mediterranean fever.

P. **Ashkenazi Jewish Genetic Panel Testing**

Ashkenazi Jewish genetic panel testing may be indicated when **ALL** of the following are present:

1. Individual to be tested is of Ashkenazi Jewish ancestry and of reproductive age.

AND

2. Panel testing is being ordered to assess for mutations associated with **3 or more** of the following diseases:

    a) Bloom syndrome
    b) Canavan disease
    c) Cystic fibrosis
    d) Dihydrolipoamide dehydrogenase deficiency
    e) Familial dysautonomia (Riley-Day syndrome)
    f) Familial hyperinsulinism
    g) Fanconi anemia group C
    h) Gaucher disease
    i) Glycogen storage disease type 1A
    j) Joubert syndrome 2
    k) Maple syrup urine disease
    l) Mucolipidosis IV
    m) Nemaline myopathy
    n) Niemann-Pick disease type A
    o) Spinal muscle atrophy
    p) Tay-Sachs disease
    q) Usher syndrome type 1F
    r) Usher syndrome type 3

Q. Spinal Muscular Atrophy (SMA)

Clinical Indications:
Spinal Muscular Atrophy genetic testing of the SMN1 and SMN2 genes may be indicated when the appropriate clinical situation is present, as indicated by 1 or more of the following:

1. Symmetric flaccid paralysis in infants

OR

2. Poor muscle tone in infants

OR

3. Lack of motor development in infants (i.e., the ability to sit without support was never achieved)

OR

4. Diffuse symmetric proximal muscle weakness that is greater in the lower than upper limbs (this may be evident by frequent falls, abnormal gait, etc.)

OR

5. Markedly decreased deep tendon reflexes

OR

6. Progressive muscle weakness

OR

7. Prospective parents who wish to reproduce

R. **Hereditary Hypertrophic Cardiomyopathy (HCM)** individual mutation diagnostic or screening testing is covered for panels up to 20 mutations: ACTC (ACTC1), CAV3, GLA, LAMP2, MTTG, MTTI, MTTK, MTTQ, MYBPC3, MYH7, MYL2, MYL3, PRKAG2, TNNC1, TNNI3, TNNT2, TPM1, TTR may be indicated when ALL of the following are present:

1. Confirmation of diagnosis in individual with clinical manifestations suggestive of hypertrophic cardiomyopathy

AND

2. The member is the first-degree relative of an individual with hypertrophic cardiomyopathy

AND

3. Testing is accompanied by genetic counseling

S. **Mucopolysaccharidosis IVA (Morquio syndrome)**

A diagnosis of Morquio A syndrome may be confirmed by the following criteria:

1. Documented clinical signs and symptoms of the disease (e.g., kyphoscoliosis, genu valgum, pectus carinatum, gait disturbance, growth deficiency, etc.)

OR

2. Documented reduced fibroblast or leukocyte GALNS enzyme activity

OR

3. Molecular genetic testing of GALNS

T. **CD40 Ligand Deficiency (also known as CD40LG or X-Linked Hyper IgM) testing**

A diagnosis of Hyper IgM syndrome may be confirmed by genetic testing when the following criteria are met:

1. The individual has at least one first- or second- degree relative with X-Linked Hyper IgM syndrome.

OR

2. The individual has an absent or decreased expression of the CD40 ligand (CD40L) protein on flow cytometry

OR

3. The individual has clinical characteristics indicative of X-linked hyper IgM syndrome (examples include, but are not limited to low serum concentrations of IgG and IgA and normal or elevated serum concentrations of IgM, neutropenia, thrombocytopenia, anemia, autoimmune and/or inflammatory disorders, or recurrent upper and lower respiratory tract bacterial infections, opportunistic infections, and recurrent or protracted diarrhea associated with failure to thrive).

U. **Hereditary Fructose Intolerance Testing (ALDOB Gene)**

For specific mutation if known in a family or panel specific mutation is unknown, based on family history and clinical features requiring a specific diagnosis

V. **Tay-Sach's** disease (**HEXA gene**) is approved for **1 or more** of the following:

a. Carrier testing for **1 or more** of the following:

1) Individual of Ashkenazi Jewish ancestry and of reproductive age

2) Individual with deficiency of beta-hexosaminidase A enzyme activity on carrier screening assay

3) Individual with family history of Tay-Sachs disease and of reproductive age, when both disease-causing mutations in HEXA gene have been identified in affected relative

4) Prior to gamete donation if gamete recipient is carrier

b. Confirmation of diagnosis of Tay-Sachs disease in symptomatic patient with inconclusive leukocyte or serum activity of beta-hexosaminidase A

c. Establishment of disease-causing mutation in patient with confirmed diagnosis of Tay-Sachs disease

d. Preimplantation genetic diagnosis when disease-causing mutation in HEXA gene has been identified in both parents

e. Prenatal diagnosis when disease-causing mutation in HEXA gene has been identified in both parents

W. **Wiskott-Aldrich syndrome (WAS)** gene mutation testing 1 or more of the following:

1. Individual is male with all of the following:
   a) Initial testing points to a WAS related disorder (Wiskott Aldrich Syndrome, X linked thrombytopenia, X-linked congenital neutropenia)
2. Individual is female with all of the following:
   a) There is a known family history of WAS gene mutation (testing is to identify female carriers)
3. Testing is prenatal with all of the following indications:
   a) Fetus is male. Testing is being done with chorionic villi sampling or cultured amniocytes
   b) There is known risk of WAS gene mutation (positive family history of WAS gene mutation and/or of known positive carrier females)

X. **Phenylalanine hydroxylase (PAH) Testing for phenylketonuria (PKU) diagnosis**

Y. **Envisia Idiopathic Pulmonary Fibrosis Diagnostic** testing is considered medically necessary for all of the following:

1. Individual has Optima Medicare or Virginia Optima Medicaid Plan
2. Individual is healthy enough to undergo bronchoscopy with transbronchial biopsies
3. High-resolution CT scan of chest demonstrates 1 or more of the following:
   a. "Probable UIP" pattern, as defined by 2018 Fleischner Society white paper
   b. "Indeterminate for UIP" pattern, as defined by 2018 Fleischner Society white paper

4. Clinical evaluation (including evaluation by rheumatologist when indicated) and serologic testing excludes autoimmune disease.
5. Absence of definitive occupational, environmental, medication-related, or other cause of patient's lung disease

Z. **McKusick-Kaufman Syndrome Single Gene Test** testing is considered medically necessary for all of the following:
1. Individual displays symptoms
2. Definitive diagnosis is uncertain
3. Test will influence treatments for disabilities and need for future care
4. Follow up laboratory testing will be required dependent on diagnosis

AA. **CYP21A genetic testing for congenital adrenal hyperplasia** testing is considered medically necessary for 1 or more of the following:

1. Completed baseline serum 17-hydroxyprogesterone (17OHP) level as borderline or elevated
2. Cosyntropin stimulation test, (ACTH stimulation test) Completed

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CPT Codes:

0018U	Oncology (thyroid), microRNA profiling by RT-PCR of 10 microRNA sequences, utilizing fine needle aspirate, algorithm reported as a positive or negative result for moderate to high risk of malignancy
0069U	Oncology (colorectal), microRNA, RT-PCR expression profiling of miR-31-3p, formalin-fixed paraffin-embedded tissue, algorithm reported as an expression score
0088U	Transplantation medicine (kidney allograft rejection) microarray gene expression profiling of 1494 genes, utilizing transplant biopsy tissue, algorithm reported as a probability score for rejection
0158U	MLH1 (mutL homolog 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
0159U	MSH2 (mutS homolog 2) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
0160U	MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
0161U	PMS2 (PMS1 homolog 2, mismatch repair system

	component) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure)
0162U	Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure)
0319U	Nephrology (renal transplant), RNA expression by select transcriptome sequencing, using pretransplant peripheral blood, algorithm reported as a risk score for early acute rejection
0320U	Nephrology (renal transplant), RNA expression by select transcriptome sequencing, using posttransplant peripheral blood, algorithm reported as a risk score for acute cellular rejection
0342U	Oncology (pancreatic cancer), multiplex immunoassay of C5, C4, cystatin C, factor B, osteoprotegerin (OPG), gelsolin, IGFBP3, CA125 and multiplex electrochemiluminescent immunoassay (ECLIA) for CA19-9, serum, diagnostic algorithm reported qualitatively as positive, negative, or borderline
81161	DMD (dystrophin) (eg, Duchenne/Becker muscular dystrophy) deletion analysis, and duplication analysis, if performed
81177	ATN1 (atrophin 1) (eg, dentatorubral-pallidoluysian atrophy) gene analysis, evaluation to detect abnormal (eg, expanded) alleles
81200	ASPA (aspartoacylase) (eg, Canavan disease) gene analysis, common variants (eg, E285A, Y231X)
81222	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; duplication/deletion variants
81224	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; intron 8 poly-T analysis (eg, male infertility)
81228	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (eg, Bacterial Artificial Chromosome [BAC] or oligo-based comparative genomic hybridization [CGH] microarray analysis)
81229	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities;
81242	FANCC (Fanconi anemia, complementation group C) (eg, Fanconi anemia, type C) gene analysis, common variant
81243	FMR1 (Fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; evaluation to detect abnormal

(eg, expanded) alleles

81244 FMR1 (Fragile X mental retardation 1) (eg, fragile X mental retardation) gene analysis; characterization of alleles (eg, expanded size and methylation status)

81255 HEXA (hexosaminidase A [alpha polypeptide]) (eg, Tay-Sachs disease) gene analysis, common variants (eg, 1278insTATC, 1421+1G>C, G269S)

81260 IKBKAP (inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase complex-associated protein) (eg, familial dysautonomia) gene analysis, common variants (eg, 2507+6T>C, R696P)

81280 Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); full sequence analysis

81281 Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); known familial sequence variant

81282 Long QT syndrome gene analyses (eg, KCNQ1, KCNH2, SCN5A, KCNE1, KCNE2, KCNJ2, CACNA1C, CAV3, SCN4B, AKAP, SNTA1, and ANK2); duplication/deletion variants

81290 MCOLN1 (mucolipin 1) (eg, Mucolipidosis, type IV) gene analysis, common variants (eg, IVS3-2A>G, del6.4kb)

81330 SMPD1(sphingomyelin phosphodiesterase 1, acid lysosomal) (eg, Niemann-Pick disease, Type A) gene analysis, common variants (eg, R496L, L302P, fsP330)

81331 **SNRPN/UBE3A** (small nuclear ribonucleoprotein polypeptide N and ubiquitin protein ligase E3A) (eg, Prader-Willi syndrome and/or Angelman syndrome), methylation analysis

81400 MOLECULAR PATHOLOGY PROCEDURE LEVEL 1 (SERPINE1 (serpine peptidase inhibitor clade E, member 1, plasminogen activator inhibitor -1, PAI-1) (eg, thrombophilia), 4G variant)

81405 MOLECULAR PATHOLOGY PROCEDURE LEVEL 6

81406 Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)

81407 Molecular pathology procedure, Level 8 (eg, analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform)

81425 Genome (eg, unexplained constitutional or heritable disorder or syndrome); sequence analysis

81479 Unlisted molecular pathology procedure

81554	Pulmonary disease (idiopathic pulmonary fibrosis [IPF]), mRNA, gene expression analysis of 190 genes, utilizing transbronchial biopsies, diagnostic algorithm reported as categorical result (eg, positive or negative for high probability of usual interstitial pneumonia [UIP])
83006	Growth stimulation expressed gene 2 (ST2, Interleukin 1 receptor like-1)
83520	Immunoassay for analyte other than infectious agent antibody or infectious agent antigen; quantitative, not otherwise specified
83529	Interleukin-6 (IL-6)
84100	Phosphorus inorganic (phosphate)
S3841	Genetic testing for retinoblastoma

See Specific Test for coverage before using the following codes:

81401	Molecular pathology procedure, Level 2
81402	Molecular pathology procedure, Level 3, gene rearrangement analysis, evaluation to detect abnormal clonal population
81403	Molecular pathology procedure, Level 4, targeted sequence analysis
81404	Molecular pathology procedure, Level 5, targeted sequence analysis
81405	Molecular pathology procedure, Level 6
81406	Molecular pathology procedure, Level 7
81408	Molecular pathology procedure, Level 9

REFERENCES

___ Agency for Healthcare Research and Quality (AHRQ)

___ Diagnostic and Therapeutic Technology Assessment (DATTA) Review

_X_ Specialty Association Guidelines

___ SHC Guidelines

_X_ Government Regulations

_X_ Literature Review

_X_ NCD

_X_ LCD

_X_ Milliman

___ Specialty Advisors

_X_ Relevant Other Payer Approaches

_X_ Winifred S. Hayes, Inc.

_X_ Uptodate

References used include but are not limited to the following:

(2019). Retrieved Dec 30, 2019, from Centers for Medicare and Medicaid Services.

(2019, Feb 11). Retrieved Dec 31, 2019, from MCG.

(2019). Retrieved Dec 30, 2019, from National Comprehensive Cancer Network.

Beygo, J., Buitine, K., Ramsden, S., Ellis, R., Clayton-Smith, J., & Kanber, D. (2019, Jun 24). Update of the EMQN/ACGS best practice guidelines for molecular analysis of Prader-Willi and Angelman syndromes. Retrieved Dec 31, 2019, from European Hournal of Human Genetics: https://www.nature.com/articles/s41431-019-0435-0

Butler, M. G., Miller, J. L., & Forster, J. L. (2019, Jun 24). Pradar-Willi Syndrome - Clinical Genetics, Diagnosis and Treatment Approaches: An Update. Retrieved Dec 31, 2019.

Clinical Guidelines Genetic Testing. (2019). Retrieved Dec 30, 2019, from AIM Specialty Health: https://aimspecialtyhealth.com/resources/clinical-guidelines/genetic-testing/

Epidemiology and genetics of Pradar-Willi syndrome. (2019, Dec 03). Retrieved Dec 30, 2019, from UpToDate.

Pradar-Willi Syndrome. (2018, Nov 30). Retrieved Dec 30, 2019, from DynaMed: https://www.dynamed.com/condition/prader-willi-syndrome-27

Carrier Screening for Genetic Conditions, Number 691. (2017, March). Retrieved October 8, 2019, from American College of Obstetricians and Gynecologists.

Clinical Appropriateness Guidelines: Genetic Testing for Reproductive Carrier Screening and Prenatal Diagnosis. (2019, September 9). Retrieved Oct 8, 2019, from AIM Specialty Health.

HEXA Gene Analysis Coding and Billing Guidelines. (2019, Jan 01). Retrieved Oct 8, 2019, from Centers for Medicare and Medicaid Services.

HGNC Data for HEXA. (2019). Retrieved October 8, 2019, from HUGO Gene Nomenclature Committee: https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:4878

Late-onset Tay–Sachs disease, Volume 17, Issue 5. (2017, October 17). doi:10.1136/practneurol-2017-001665

NCCN Guidelines. (2019). Retrieved Oct 8, 2019, from National Comprehensive Cancer Network: https://www.nccn.org/professionals/physician_gls/default.aspx

Preconception and Prenatal Carrier Screening for Genetic Disease More Common in the Ashkenazi Jewish Population and Others With A Family History Of These Disorders. (2019, Aug 1). Retrieved Oct 8, 2019, from UpToDate:

Prenatal Diagnosis of Tay-Sachs Disease, MIMB, volume 1885. (2018, December 1). doi:10.1007/978-1-4939-8889-1_16

Tay - Sachs Disease (TSD) Testing in Individuals of Non–Ashkenazi Jewish Origin. (2014, December 12). Retrieved Oct 8, 2019, from Hayes, Inc.

Tay-Sachs Disease. (2018, November 30). Retrieved Oct 8, 2019, from DynaMed Plus.

Tay - Sachs disease and Variants - HEXA Gene, ACG: A-0614 (AC). (2019, Feb 11). Retrieved Oct 8, 2019, from MCG: https://careweb.careguidelines.com/ed23/index.html

23rd Edition. (2019). Retrieved October 9, 2019, from MCG: https://careweb.careguidelines.com/ed23/index.html

(2019). Retrieved October 9, 2019, from U.S Food and Drug Administration: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/

(2019). Retrieved October 9, 2019, from Centers for Medicare & Medicaid Services: https://www.cms.gov/medicare-coverage-database/search/search-results.aspx?SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=BC%7cSAD%7cRTC%7cReg&PolicyType=Both&s=53&KeyWord=SHOX&KeyWordLookUp=Title&Key

(2019). Retrieved October 9, 2019, from National Comprehensive Cancer Network: https://www.nccn.org/professionals/physician_gls/default.aspx

Clinical Appropriateness Guidelines: Genetic Testing for Single-Gene and Multifactorial Conditions. (2019, September 9). Retrieved October 9, 2019, from AIM Specialty Health: https://aimspecialtyhealth.com/wp-content/uploads/2019/07/SingleGeneandMultifactorialConditions_Sep_2019.pdf

Genetic Evaluation of Short Stature. (2009, June). Retrieved October 10, 2019, from ACMG PRACTICE GUIDELINES: https://www.acmg.net/PDFLibrary/Short-Stature-Genetic-Evaluation.pdf

Improving Clinical Diagnosis in SHOX Deficiency: The Importance of Growth Velocity. (2018, February 1). doi:10.1038/pr.2017.247

Leri-Weill Dyschondrosteosis. (2014, July 31). Retrieved October 9, 2019, from Hayes: https://evidence.hayesinc.com/report/gte.leri2259

Recurrent Copy Number Variants Associated with Syndromic Short Stature of Unknown Cause. (2017, November 9). Hormone Research In, 13-21. doi:10.1159/000481777

Search Results for SHOX. (2019, January 1). Retrieved October 9, 2019, from EncoderPro: https://www.encoderpro.com/epro/baseSearchHandler.do?mainsearchtype=code&searchContextOption=49167&searchTerms=shox&_a=search&forwardURL=%2FcptHandler.do%3F_mrad%3Dtrue%26_a%3Dview%26_k%3D101*81405&org.apache.struts.taglib.html.TOKEN=4bbe1598-826a-40e7-8a

Sex Chromosome Abnormalities, 10.0. (2019, March 1). Retrieved October 9, 2019, from UpToDate: https://www.uptodate.com/contents/sex-chromosome-abnormalities?search=SHOX%20testing&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3

Short Stature in Children - Approach to the Patient. (2018, November 30). Retrieved October 9, 2019, from DynaMed: https://www.dynamed.com/approach-to/short-stature-in-children-approach-to-the-patient#GUID-ABB14936-7324-45B5-BBA4-DB47FBF35501

SHOX Deficiency. (2017). Retrieved October 10, 2019, from Child Growth Foundation: https://childgrowthfoundation.org/conditions/shox/

SHOX Deficiency Disorders. (2018, June 28). Retrieved October 10, 2019, from U.S. National Library of Medicine: GeneReviews: https://www.ncbi.nlm.nih.gov/books/NBK1215/

Morrow, D, Sweeney, C, Birney, YA, et al. Cyclic strain inhibits Notch receptor signaling in vascular smooth muscle cells in vitro. Circ Res 2005; 96:567.

Joutel, A, Monet, M, Domenga, V, et al. Pathogenic mutations associated with cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy differently affect Jagged1 binding and Notch3 activity via the RBP/JK signaling Pathway. Am J Hum Genet 2004; 74:338.

Peters, N, Opherk, C, Zacherle, S, et al. CADASIL-associated Notch3 mutations have differential effects both on ligand binding and ligand-induced Notch3 receptor signaling through RBP-Jk. Exp Cell Res 2004; 299:454.

Lesnik Oberstein, SA, van den Boom, R, van Buchem, MA, et al. Cerebral microbleeds in CADASIL. Neurology 2001; 57:1066.

Joutel, A, Chabriat, H, Vahedi, K, et al. Splice site mutation causing a seven amino acid Notch3 in-frame deletion in CADASIL. Neurology 2000; 54:1874.

Arboleda-Velasquez, JF, Lopera, F, Lopez, E, et al. C455R notch3 mutation in a Colombian CADASIL kindred with early onset of stroke. Neurology 2002; 59:277.

Goldenberg I, Moss AJ. Long QT syndrome. Journal of the American College of Cardiology 2008; 51(24):2291-300. DOI: 10.1016/j.jacc.2008.02.068.

Morita H, Wu J, Zipes DP. The QT syndromes: long and short. Lancet 2008; 372(9640):750-63. DOI: 10.1016/S0140-6736(08)61307-0.

Genetic testing for long QT syndrome. Technology Evaluation Center Assessment Program. Executive Summary 2008; 22(9):1-5.

Roden DM. Clinical practice. Long-QT syndrome. New England Journal of Medicine 2008; 358(2):169-76. DOI: 10.1056/NEJMcp0706513

Shimizu W. Clinical impact of genetic studies in lethal inherited cardiac arrhythmias. Circulation Journal 2008; 72(12):1926-36.

Moskowitz SM, et al. Clinical practice and genetic counseling for cystic fibrosis and CFTR-related disorders. Genetics in Medicine 2008; 10(12):851-68. DOI: 10.1097/GIM.0b013e31818e55a2.

Dequeker E, et al. Best practice guidelines for molecular genetic diagnosis of cystic fibrosis and CFTR-related disorders--updated European recommendations. European Journal of Human Genetics 2009; 17(1):51-65. DOI: 10.1038/ejhg.2008.136.

Farrell PM, et al. Guidelines for diagnosis of cystic fibrosis in newborns through older adults: Cystic Fibrosis Foundation consensus report. Journal of Pediatrics 2008; 153(2):S4-S14. DOI: 10.1016/j.jpeds.2008.05.005.

Miller IO, Sotero de Menezes MA. SCN1A-Related Seizure Disorders. 2007 Nov 29 [Updated 2014 May 15]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2014. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1318/

Hisama FM, Dib-Hajj SD, Waxman SG. SCN9A-Related Inherited Erythromelalgia. 2006 May 6 [Updated 2013 Aug 15]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2014. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1163/

Scheffer, I., (2011). Genetic testing in epilepsy: What should you be doing? Epilepsy Currents, Vol. 11, No. 4 (July/August) 2011 pp. 107–11. Access available at: https://www.aesnet.org/sites/default/files/file_attach/ProfessionalEducation/Currents/2011/Vol11num4/11-4-107 Basic Review Scheffer.pdf.

Wuyts W, Schmale GA, Chansky HA, et al. Hereditary Multiple Osteochondromas. 2000 Aug 3 [Updated 2013 Nov 21]. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2015. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1235/